Nuclear Magnetic Resonance Spectroscopy. Kinetics of Isomerization of Para-Substituted Hexafluoroacetone *N*-Phenylimines[1]

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Abstract: The kinetics of the degenerate isomerization about the carbon–nitrogen double bond of hexafluoroacetone *N*-phenylimine and its *p*-chloro, *p*-fluoro, *p*-methoxy, *p*-methyl, and *p*-nitro derivatives have been studied by line-shape analysis of nmr spectra at a series of temperatures. The free energies of activation at 25° were found to be 15.45, 15.53, 15.35, 14.35, 15.14, and 14.90 kcal mol^{-1}, respectively. With the exception of the *p*-nitro compound, the rate constants at 25° give a Hammett plot with a linear correlation coefficient of 0.989 when σ^+ substituent constants are used; the ρ value is -0.980. The results are interpreted as being the consequence of an in-plane inversion about the imine nitrogen of the *p*-nitro compound and a rotation about the imine carbon–nitrogen bond of the others.

Cis–trans (or syn–anti) isomerization about a carbon–nitrogen double bond has been investigated for a variety of compounds,[5-21] and a remarkable range of rates, at least 16 powers of 10, has been found for this reaction.[19] Two mechanisms are commonly invoked: a rotation of the N substituent out of the plane of the molecule,[12,14,20a] as in cis–trans isomerization about a carbon–carbon double bond, or an in-plane "lateral shift,"[5a,9,11,13,16,18,19,20b] comparable to inversion about nitrogen in amines.[22] The rate is sensitive to substituents at either side of the carbon–nitrogen bond and the effects of groups on both the carbon[11,19,24] and the nitrogen[5,13,18-20] have been examined. Of the latter, the effect of substituents (Z) on the phenyl group of imines of the type $X_1X_2C{=}N\text{-}C_6H_4Z$, where $X_1 = X_2 = CH_3O$,[20] $(CH_3)_2N$,[5,13] and *p*-$CH_3OC_6H_4$,[19] and where $X_1 = H$, $X_2 = C_6H_5$[21] and $X_1 = C_6H_5$, $X_2 =$ *p*-$CH_3OC_6H_4$[19] have been reported. All of these series contain X groups which may participate by resonance interaction with the carbon–nitrogen double bond. We now report a study of the kinetics of the degenerate isomerization of six para-substituted hexafluoroacetone *N*-phenylimines where $X_1 = X_2 = CF_3$, a group expected to have a strong inductive effect but little resonance interaction.

Results

The low-temperature fluorine nmr spectrum of each of the compounds in pyridine or acetone consists of two absorptions of equal intensity, each split into a quartet by four-bond coupling with the other trifluoromethyl group (see Table I). The chemical-shift differences change only slightly with temperature. As the temperature is raised, the absorption bands first lose their fine structure, then coalesce to a singlet. These simple A_3B_3 spectra permit the determination of rates in two regions, coalescence at higher temperature and loss of fine structure at lower temperature, thus offering the advantage recently emphasized by Binsch of two ". . . individual clocks, running in different time scales . . ."[25] The accessibility of the two regions is fortunate, for the precision of the results from either alone would not be high: in the higher temperature range the chemical-shift difference is so large that the peak height and signal-to-noise ratio are small in the coalescence region, while in the lower range the loss of the spin–spin splitting by chemical-shift averaging is rather less sensitive to the rate change than is the collapse of a multiplet by averaging of spin states through exchange of nuclei.[26]

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Table I. Fluorine Nmr Values. Para-Substituted Hexafluoroacetone *N*-Phenylimines $(CF_3)_2C{=}NC_6H_4Z^a$

	Substituent Z					
	H	Cl	F	OCH_3	CH_3	NO_2
Difference in chemical shifts, corrected to 0°, Hz	434	429	419	367	416	430
Change in shift difference with temperature, Hz deg^{-1}	−0.11	−0.09	−0.05	−0.04	−0.05	0.01
Coupling constant, $^4J_{FF}$, Hz	7.1	6.9	6.9	7.2	6.9	6.6

[a] At 56.4 MHz, 33% pyridine solution.

Table II. Kinetic Values, Isomerization of Para-Substituted *N*-Phenylimines, $(CF_3)_2C{=}NC_6H_4Z$

	Substituent Z						
	H	Cl	F	OCH_3	NO_2	CH_3	$CH_3{}^f$
Log *A*	12.2 ± 0.1[e]	13.0 ± 0.1	13.0 ± 0.1	12.6 ± 0.1	12.3 ± 0.1	12.7 ± 0.1	12.5 ± 0.1
E^a	14.6 ± 0.2	15.8 ± 0.1	15.7 ± 0.1	14.1 ± 0.2	14.2 ± 0.2	15.1 ± 0.1	14.7 ± 0.2
$\Delta G^{\ddagger\,a,b}$	15.45 ± 0.02	15.53 ± 0.02	15.35 ± 0.01	14.35 ± 0.02	14.90 ± 0.02	15.14 ± 0.01	15.14 ± 0.02
$\Delta H^{\ddagger\,a}$	14.0 ± 0.2	15.2 ± 0.1	15.1 ± 0.1	13.5 ± 0.2	13.6 ± 0.2	14.5 ± 0.1	14.1 ± 0.2
$\Delta S^{\ddagger\,c}$	−4.9 ± 0.6	−1.1 ± 0.4	−0.9 ± 0.4	−2.9 ± 0.6	−4.2 ± 0.6	−2.3 ± 0.4	−3.4 ± 0.5
Number of points, σ^d	10, 0.91	11, 0.65	11, 0.61	10, 0.87	13, 0.62	16, 0.60	10, 0.74
Log $k^{b,g}$	1.47 ± 0.01	1.41 ± 0.01	1.54 ± 0.01	2.28 ± 0.01	1.87 ± 0.01	1.69 ± 0.01	1.69 ± 0.01

[a] In kcal mol^{-1}. [b] At 25°. [c] In eu. [d] σ is the root mean square of the weighted residuals. [e] Uncertainties are the 50% confidence limits. [f] In methylcyclohexane. All other data are for pyridine solutions. [g] Calculated from $\Delta G^{\ddagger}$.

The addition of either hydrochloric acid (trace or 2 *N*) or sodium hydroxide (trace) had no effect upon the spectrum of hexafluoroacetone *N*-(*p*-methylphenyl)-imine in acetone at ambient temperature (~40°), demonstrating freedom from any strong acid or base catalysis. Pyridine was the solvent used for the kinetic study of the series: many samples darkened on standing in acetone; the *p*-nitro compound was not sufficiently soluble in methylcyclohexane. There was essentially no difference in the kinetic results for the *p*-methyl compound, whether in pyridine or in methylcyclohexane (see Table II).

The first-order rate constants for isomerization were determined by matching calculated and observed spectra at specific temperatures. The calculated spectra were obtained from the Binsch DNMR program.[27] The actual six-spin system exceeded the four-spin limitation of this program, necessitating the use of smaller spin systems for the computations. For the collapse of the quartets, a single fluorine coupled with three others by the experimental *J* value was taken as the model; for the coalescence of the bands, two uncoupled fluorines with chemical-shift differences corrected to the appropriate temperature were used. It is not certain what line width should be taken for T_2 (effective transverse relaxation time) for the latter case. We used $3J + W$ where *J* is the coupling constant of the fluorines and *W* is the width at half-height of the peak of the internal standard, 1,1,1-trifluoro-2,2,2-trichloroethane. However, the large difference in chemical shifts makes the line shape at, and near, coalescence insensitive to line width of the individual peaks. Therefore, we consider any error introduced by errors in our assumed value of the line width to be insignificant. Figure 1 shows a comparison of the experimental and calculated spectra of hexafluoroacetone *N*-(*p*-fluorophenyl)imine.

The kinetic parameters were calculated from the rate constants by a FORTRAN program (ARH2).[28] This program weights the experimental points inversely to the uncertainties in rate constant and temperature, and for a specified temperature, finds the enthalpy and entropy of activation that give the best fit to the linear equation (1) from the absolute reaction rate theory.[29] The results are shown in Table II and Figure 2.

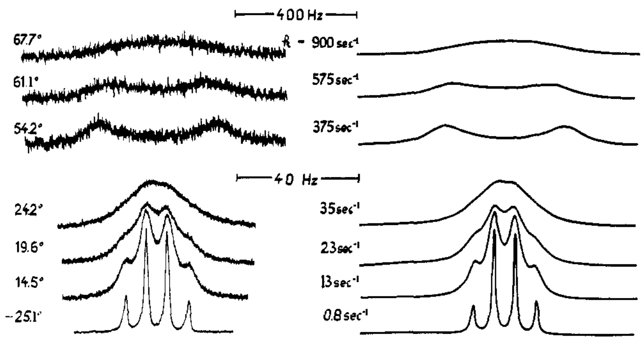

Figure 1. Temperature dependence of the fluorine nmr spectrum of hexafluoroacetone *N*-(*p*-fluorophenyl)imine, 33% solution in pyridine, 56.4 MHz. The portions of the spectra at 54.2° and above are of the two trifluoromethyl groups, while the spectra at below 54.2° are of the upfield trifluoromethyl group. The spectrum amplitude is not constant. Experimental spectra to the left, calculated to the right.

$$\ln(k/T) = \ln(k/h) + \Delta S^{\ddagger}/R - (\Delta H^{\ddagger}/R)1/T \quad (1)$$

Discussion

The isomerization of an imine about the carbon–nitrogen double bond by rotation can be represented by **1**, and by the lateral shift mechanism as in **2**. In **1**, Y

Nuclear Magnetic Resonance Spectroscopy," Pergamon Press, New York, N. Y., 1965, pp 494-496.

(27) G. Binsch, *J. Amer. Chem. Soc.*, **91**, 1304 (1969). We thank Dr. B. L. Hawkins for the use of his version of this program which is set up for an IBM 360/75 computer.

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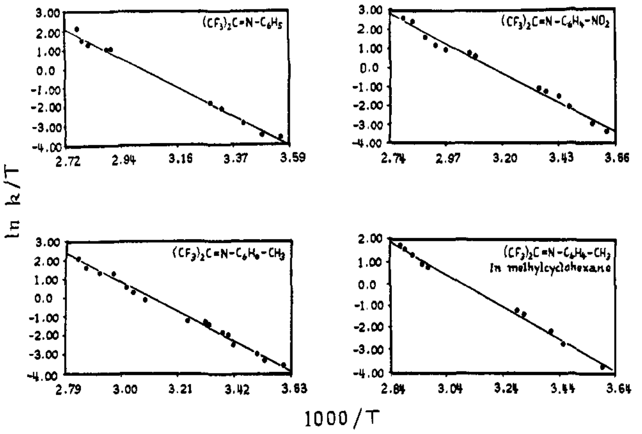
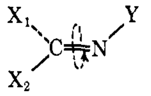


Figure 2. Illustrative Eyring plots of the kinetic data for imine isomerization in pyridine.



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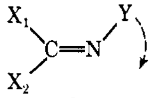

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rotates out of the plane of the molecule; in **2**, Y moves through a linear C–N–Y position while remaining in the plane of the molecule. Attempts to choose between these mechanisms have sometimes given conflicting results. Thus, isomerization of the dianil of *p*-benzoquinone is facile even after conversion to the di-*N*-oxide. The binding of the nitrogen electron pair on oxide formation prevents inversion, or lateral shift, and requires a rotation mechanism.[14] On the other hand, similar reasoning requires the lateral shift mechanism for the isomerization of acetophenone *N*-phenylimine; isomerization ceases when this substance is complexed with aluminum chloride.[9] Marullo and Wagener[20a] interpreted the inversion of iminocarbonates ($X_1 = X_2 = CH_3O$) on the basis of rotation; Leibfritz and Kessler[20b] and Vögtle, Mannschreck, and Stabb[17] favored a lateral shift for iminocarbonates and iminothiocarbonates, while Marullo and Wagener[12] reply that if bond participation in lateral shift is included, a choice cannot be made on the basis of electronic effects.

One approach to an understanding of this isomerization has been through the application of the Hammett free energy relationship[30] to imines bearing phenyl substituents. Substitution in a phenyl group attached to nitrogen has a greater effect than in one attached to carbon (ρ's of $+1.5$[19] and $+2.0$[21] have been reported for the former, $+0.1$[24] and $+0.4$[21] for the latter). The increased facility of isomerization with electron-withdrawing groups, as indicated by the positive sign of ρ, is consistent with a transition state of type **3**.[9,19] Where either X_1 or X_2 is capable of resonance interaction with the carbon–nitrogen double bond, a positive sign of ρ is also in accord with a rotational transition state of type **5**.

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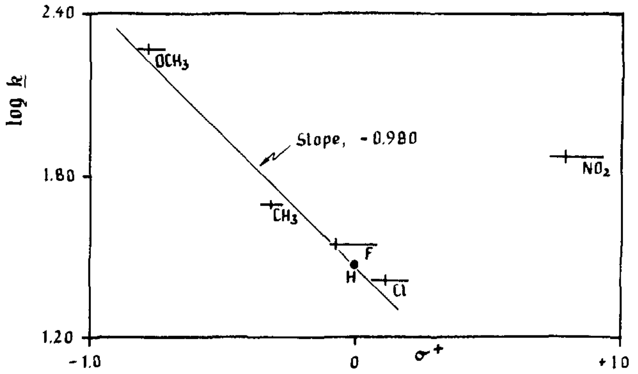
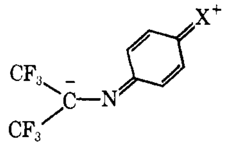


Figure 3. Hammett plot for rate of isomerization (k) of para-substituted hexafluoroacetone *N*-phenylimines, using σ^+ substituent constants.[30] The uncertainties in log k correspond to the calculated errors in $\Delta G^{\ddagger}$ (Table II). The ranges of σ^+ values are from H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, **80**, 4979 (1958); the best values are those for the standard reaction.

The influence of substituents on the phenyl group of hexafluoroacetone *N*-phenylimine is in marked contrast to that reported for other imines: the isomerization is facilitated by electron-donating substituents. The points in a plot of log k (25°) *vs.* the σ constants for the substituents[30] fall roughly on a straight line, with the exception of the widely divergent point for the *p*-nitro compound; the linear correlation coefficient for a least-squares line, omitting the nitro compound, is 0.845. When σ^+ values[30] are used in place of σ (Figure 3), the linear correlation coefficient rises to 0.989, again with the omission of the nitro compound. The slope of the line, and hence the value of ρ for the reaction, is -0.980. The value of log k for the *p*-nitro compound is 1.174 greater than would be predicted from the least-squares fit for the other compounds; the rate constant at 25° is larger by a factor of 15. The free energies of activation are too low for a mechanism involving homolytic cleavage of one of the carbon–nitrogen bonds, where activation energies in the range of 40–60 kcal mol^{-1} are to be expected.[16] The mechanism for the *p*-nitro compound must be different from that for the other five. The better fit to the Hammett equation with σ^+ than with σ substituent constants, nitro excluded, indicates that resonance is important in the process which supplies electrons and favors formation of the transition state. A transition state of type **3** for the nitro derivative and of type **4** for the other five compounds is consistent with these findings. The small values of the entropies of activation and the essential equivalence of pyridine and methylcyclohexane solutions rule out any important solvent participation by these low-polarity solvents.[31]



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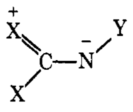
[30] L. P. Hammett, "Physical Organic Chemistry," 2nd ed, McGraw-Hill, New York, N. Y., 1970, Chapter 11.

[31] A referee has suggested that solvent participation in the *p*-nitro compound through the intermediacy of **4a** may be an alternative explanation for the change in mechanism with this derivative. The *p*-nitro compound would be the most electron deficient at the imine carbon and

The difference in transition state for the five hexafluoroacetone *N*-phenylimines from that found for other *N*-phenylimines (**3**) may arise from the strong electronegative character of the trifluoromethyl group which favors a type **4** transition state wherever the phenyl group can stabilize such a charge distribution. Unfortunately, the other X groups on carbon that have been studied, R_2N, RO, RS, offer no test of this proposition, for they have unshared electron pairs on the heteroatoms that permit resonance stabilization of another type of transition state, **5**,[20] reflected in their lower activation energies. The difference in the kinetic values for the *p*-nitro compound may result from the contribution of resonance structure **6**[19] to a type **3** transition state, this stabilization being sufficient to overcome the unfavorable positive charge on the imine nitrogen adjacent to the hexafluoropropylidene group. Other explanations for our results can be devised. Whether our series offers examples of isomerization by both rotation and lateral shifts is a difficult question. Curtin and coworkers suggest that a continuum of mechanisms between the two extremes is possible;[19] Raban[6] points out that such a continuum results from varying the angle θ (**7**) in the transition state between the 109° of sp^3 hybridization and the 180° of sp hybridization. The relatively low magnitude of the Hammett ρ value for the present series, excluding the nitro compound, as compared to the values reported for the majority of other reactions where σ^+ constants give the best correlations[32] makes it clear that the transition state is reached before the development of the full charges is indicated in **4**, and may even indicate a transition state with some inversion character, *i.e.*, **7** where θ is greater than 120°. However, if the transition state is intermediate between the ground state and **4**, the extent of charge development need have no effect on geometry, for the nitrogen can retain an sp^2 hybridization throughout.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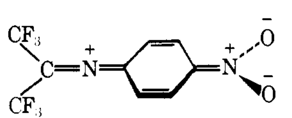
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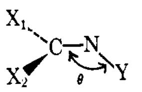
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Experimental Section

Preparation of *N*-Phenylimines. Hexafluoroacetone *N*-phenylimine was prepared by the reaction of hexafluoroacetone with phenyl isocyanate, using triphenylphosphine oxide as catalyst, according to the method of Zeifman, Gambaryan, and Knunyants.[33] The para-substituted *N*-phenylimines were prepared similarly by reaction of hexafluoroacetone with the corresponding para-substituted isocyanates, as illustrated by the following procedure.

Hexafluoroacetone *N*-(*p*-Nitrophenyl)imine. A mixture of 33 g (0.2 mol) of *p*-nitrophenyl isocyanate, 50 g (0.27 mol) of hexafluoroacetone, and 5.0 g (0.018 mol) of triphenylphosphine oxide was heated at 100° for 2 hr, 150° for 2 hr, and 200° for 4 hr in a 240-ml "Hastelloy" tube. The tube was cooled and vented, and the contents were distilled to give 54.85 g (96% yield) of the imine as a light-yellow liquid, bp 94.5–95° (4.9 mm), that solidified after a few hours to a light-yellow solid: mp 34°; uv (cyclohexane) λ_{max} 327 mμ (ϵ 2200), 267 (7600), and 216 (11,000).

Anal. Calcd for $C_9H_4F_6N_2O_2$: C, 37.78; H, 1.14; F, 39.84; N, 9.79. Found: C, 37.90; H, 1.47; F, 39.63; N, 9.53.

Hexafluoroacetone *N*-(*p*-fluorophenyl)imine (bp 63–64° (30 mm), $n^{25}\text{D}$ 1.4086) was prepared in 85% yield from *p*-fluorophenyl isocyanate.

Anal. Calcd for $C_9H_4F_7N$: C, 41.70; H, 1.56; F, 51.33; N, 5.41. Found: C, 41.52; H, 1.59; F, 51.49; N, 5.47.

Hexafluoroacetone *N*-(*p*-chlorophenyl)imine (bp 68–69° (8.6 mm), $n^{25}\text{D}$ 1.4428) was prepared in 60% yield from *p*-chlorophenyl isocyanate.

Anal. Calcd for $C_9H_4ClF_6N$: C, 39.21; H, 1.46; Cl, 12.87; F, 41.32; N, 5.10. Found: C, 39.29; H, 1.56; Cl, 12.97; F, 41.58; N, 5.22.

Hexafluoroacetone *N*-*p*-tolylimine (bp 76.5–77° (30 mm), $n^{25}\text{D}$ 1.4279, uv (ethanol) λ_{max} 348 mμ (ϵ 2240), 238 (4250), 219 (8550)) was prepared in 50% yield from *p*-tolyl isocyanate.

Anal. Calcd for $C_{10}H_7F_6N$: C, 47.05; H, 2.77; F, 44.66; N, 5.49. Found: C, 46.92; H, 2.89; F, 44.66; N, 5.51.

Hexafluoroacetone *N*-(*p*-methoxyphenyl)imine (bp 79–80° (9.8 mm), $n^{25}\text{D}$ 1.4575, uv (cyclohexane) λ_{max} 353 mμ (ϵ 4060), 242 (5860), 226 (8380)) was prepared in 85% yield from *p*-methoxyphenyl isocyanate.

Anal. Calcd for $C_{10}H_7F_6NO$: C, 44.29; H, 2.61; F, 42.04; N, 5.17. Found: C, 44.48; H, 2.62; F, 41.81; N, 5.34.

Nuclear magnetic resonance spectral measurements were made with a Varian A-56/60 spectrometer equipped with a variable-temperature probe. The pyridine solutions were 33% v/v and contained internal 1,1,1-trifluoro-2,2,2-trichloroethane for determination of natural line widths. Frequency scales were calibrated by the side-band technique. Temperatures were determined by proton peak separations of acidified methanol or ethylene glycol in sealed capillaries centered in the sample tubes by Teflon washers, using the equations of Van Geet,[34] and are believed to be accurate to ±1°. Five or more spectra were recorded at approximately 4° intervals in the vicinity of each "coalescence" temperature, at 100-Hz sweep widths at the lower range, 1000 Hz at the higher. Two 1000-Hz sweep width spectra were recorded at temperatures where the isomerization was frozen out to determine change in chemical-shift difference with temperature, and one 100-Hz sweep width at low temperature to determine the coupling constant. Accurate phasing was essential for line shape fitting about the lower "coalescence" point; where there was doubt, several spectra were recorded differing only in slight changes in the phasing.

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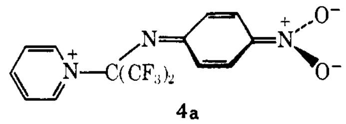
thus most susceptible to attack. No test of the effect of solvent or of added acid or base was made with this particular compound. While as small a value of $\Delta S^{\ddagger}$ (−5 eu) as found here would appear to rule out such a mechanism, the possibility that this value is in error cannot be entirely excluded: complete line-shape analyses have given erroneous $\Delta S^{\ddagger}$ values in the past. (See A. Allerhand, F. Chen, and H. S. Gutowsky, *J. Chem. Phys.*, **42**, 3040 (1965).) However, with the wide temperature range covered here it seems unlikely that $\Delta S^{\ddagger}$ could have a value on the order of −20 eu as required by solvent participation.


4a

[32] (a) L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, **1**, 35 (1963). Note, however, that the reactions considered in this reference involve a charge directly on the phenyl group rather than on a substituent: (b) P. R. Wells, *Chem. Rev.*, **63**, 171 (1963).

[33] Yu. V. Zeifman, N. P. Gambaryan, and I. L. Knunyants, *Dokl. Akad. Nauk SSSR*, **153**, 1334 (1963).

[34] A. L. Van Geet, *Anal. Chem.*, **42**, 679 (1970); **40**, 227 (1968).